Cell Therapy In Dermatology

Essay

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in Dermatology and Venereology

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رَبَّنَا آمَنَّا بِمَا أَنْزَلْتَ وَاتَّبَعْنَا الرَّسُولَ فَاكْتُبْنَا مَعَ الشَّاهِدِينَ. ال عمران(53)

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2-Chronic Lymphocytic Leukemia	Transfer of Genetically Modified T lymphocytes.

ADSCs: Adipose Derived Stem Cells.
CAL: Cell Assisted Lipotransfer.
CD4: cluster of differentiation 4.
CTL:cytolytic T lymphocytes.
DCs:Dendritic Cells .
EPC: Endothelial Progenitor Cells.
HSCT: Hematopoietic stem cell transplantation.
MSCs: mesenchymal stem cells.
NSCs :neural stem cells.
PBSCT: peripheral blood stem cell transplant .
PRP: Platelet Rich Plasma.
SKP: skin-derived precursor .
VEGF: Vascular Endothelial Growth Factor.

List of Abbreviations

- ACEI: Angiotensin Converting Enzyme Inhibitors .
- ACR: autologous cell regeneration.
- ADSCs: Adipose Derived Stem Cells.
- AIDS:Acquired Immune Deficiency Syndrome.
- BFGF :Basic Fibroblast Growth Factor.
- BMP7: bone morphogenetic protein 7.
- BMP10: bone morphogenetic protein 10.
- BMZ:Basement membrane zone.
- CA: carbonic anhydrase.
- CAL: Cell Assisted Lipotransfer.
- CD4: cluster of differentiation 4.
- CD8: cluster of differentiation 8.
- CLL: chronic lymphocytic leukemia.
- CNS:Central Nervous System.
- CT: computed tomography.
- CTL:cytolytic T lymphocytes.
- DCs:Dendritic Cells .
- DEJ: dermal-epidermal junction.
-DP: Dermal papiller.
-DS: dermal sheath.
- EB: Epidermolysis bullosa
- EBV: Epstein-Barr virus .
- ECM :Extracellular matrix .

- EGF: Epidermal Growth Factor.
- E/M: Electron microscopy.
- EPC: Endothelial Progenitor Cells.
- ESCs: Embryonic Stem Cells.
- EULAR/EBMT :European League Against Rheumatism and European Group for Blood and Marrow Transplantation .
- FDA: Food and Drug Administration.
- FMSCs: Fibroblast Mesenchymal Stem Cells.
- GFP :green fluorescent protein.
- GIT:Gastrointestinal tract.
- GMCSF:Granulocyte-macrophage colony-stimulating factor.
- GVHD :Graft-versus-host disease .
- HDMEC: Human Dermal Microvascular Endothelial Cells.
- H2O2: Hydrogen peroxide.
- HLA :Human leukocyte antigen.
- HSCs: Hematopoietic Stem Cells.
- HSCT: Hematopoietic stem cell transplantation.
- ICX-RHY: Intercytex.
- IFN g:Interferon gamma.
- Igs :immunoglobulins.
- IL 4: interleukin 4.
- IPL: Intense pulsed light.
- LIF: Leukemia Inhibitory Factor.
- LMP2: latent membrane protein 2 .
- mAb: monoclonal antibody.

- MAGEA: Melanoma antigen family A.
- MSCs: mesenchymal stem cells.
- NICE:National Institute for Health and Clinical Evidence.
- NP:nucleus pulposus.
- NPC :Nasopharyngeal carcinoma.
- NSAIDs :Nonsteroidal anti-inflammatory drugs .
- NSCs :neural stem cells.
- PASI: Psoriasis Area and Severity Index.
- PBS: Phosphate Buffer Saline.
- PBSCT: peripheral blood stem cell transplant .
- PCAs :Primary cicatricial alopecias .
- PDGF: Platelet Derived Growth Factor.
- PMMA: Polymethylmethacrylate.
- PNs:Purkinje Neurones.
- PRP: Platelet Rich Plasma.
- PUVA :psoralen UV-A .
- RCC :Renal cell carcinoma.
- RDEB: Recessive dystrophic epidermolysis bullosa.
- ROS: Reactive oxygen species .
- RT-PCR: Reverse transcription polymerase chain reaction .
- SCNT: Somatic Cell Nuclear Transfer.
- SKP: skin-derived precursor .
- SSc:Systemic sclerosis.
- SSCs: Somatic Stem Cells.
- SVF: stromal vascular fraction .

- TAA:Tumor associated antigens.
- TGF: Transforming Growth Factor .
- TKIs: tyrosine kinase inhibitors .
- TNFα :Tumor necrosis factor alpha.
- tPA:tissue Plasminogen Activator.
- TRM: transplant related mortality.
- UV:Ultra Violet.
- VEGF: Vascular Endothelial Growth Factor.
- κ: kappa .
- λ :lambda.

Introduction

Introduction

Cell therapy is the transplantation of human or animal cells to replace or repair damaged tissue and/or cells. Cell therapy is, in effect, a type of organ transplant. The procedure involves the injection of either whole fetal xenogenic (animal) cells or cell extracts from human tissue. The latter is known as autologous cell therapy if the cells are extracted from and transplanted back into the same patient.Cell therapy has been used successfully to rebuild damaged cartilage in joints, repair spinal cord injuries, strengthen a weakened immune system, treat autoimmune diseases such as Acquired Immune Deficiency Syndrome (AIDS) , and to help patients with neurological disorders such as Alzheimer's disease , Parkinson's disease , and epilepsy ***(Martin,2007).***

Cell therapy has proven efficacy in many fields. New insights into the biology of neural stem cells (NSCs) have raised expectations for their use in the treatment of neurologic diseases. Originally, NSC transplantation was proposed as a means of replacing cells in central nervous system (CNS) diseases that result in cell loss ***(Einstein and Ben-Hur ,2008).*** Studies performed by ***Abbah et al.,2008*** and ***Zhang et al.,2008*** demonstrated the ability of transduced articular chondrocytes to survive and promote proteoglycan accumulation when transplanted into the intervertebral discs. These data support the potential of a cell-based gene therapy approach for disc repair***.***

One of the fields of medicine that has raised the most expectations in recent years is cell therapy with stem cells. The isolation of human embryo cells, the apparent and unexpected potentiality of adult stem cells and the development of gene therapy lead to imagine a hopeful future for a significant number of diseases that are at present incurable ***(Martin,2007).***

In the field of dermatology, tumor-associated antigens (TAA) are promising candidates as target molecules for immunotherapy and a wide variety of tumor-associated antigens have been discovered through the presence of serum antibodies in cancer patients. Conduction of dendritic cell therapy on malignant melanoma

patients proved shrinkage or disappearance of metastatic tumors **(*Yoshiura et al.,2005).*** Cell vaccination therapy in melanoma has now many years of experience. Initially, the treatment was based on the use of autologous or allogeneic inactivated tumor cells. This depends on the antigenicity of human tumor cells, which can be recognized by T lymphocytes and particularly by cytolytic T lymphocytes (CTL). This antigenicity of tumor cells lead to the development of therapeutic anti-cancer vaccines that induce tumor regressions or prevent the development of metastases in the vaccinated patients, with metastatic melanoma. Detailed immunological analyses with some of these vaccinated patients showed strong anti-tumor T cell responses and suggested that the main limiting factor for clinical efficacy is a phenomenon of resistance of the tumor to T lymphocyte attack ***(Baurain et al.,2008).***

Scleroderma has an autoimmune-related pathogenesis, particularly in early illness. In this disease, stem cell therapy is a reasonable potential choice. Hematopoietic stem cell transplantation has being tested in prospective randomized controlled trials and appears to reset autoimmunity in systemic sclerosis (Ssc). Mesenchymal stem cells (MSC) may have an immunomodulatory role in autoimmune diseases such as scleroderma (***Tyndall and Furst ,2007).***

Recessive dystrophic epidermolysis bullosa (RDEB) is a severe inherited skin-blistering disorder caused by mutations in the COL7A1 gene that lead to reduced type-VII collagen and defective anchoring fibrils at the dermal-epidermal junction (DEJ). Presently there are no effective treatments for this disorder. Many studies have shown that intradermal injections of normal human fibroblasts can generate new human type-VII collagen and anchoring fibrils at the DEJ***(Wong et al.,2008).***

Most low grade lymphoma and chronic lymphocytic leukemia cells express monoclonal immunoglobulins (Igs) carrying either kappa (κ)or lambda (λ) light chains. T lymphocytes could be genetically modified to target the tumor-associated light chain, sparing B lymphocytes expressing the reciprocal light chain, and consequently reduce impairment of humoral immunity.T lymphocytes expressing the anti-kappa light chain showed

cytotoxic activity against Ig kappa positive tumor cell lines both in vitro and in vivo ***(Vera et al.,2006).***

Treatment of severe radiation burns remains a difficult challenge. Conventional surgical treatment (excision, skin grafting, skin or muscle flaps) often fails to prevent unpredictable and uncontrolled extension of the necrotic process. Some clinical cases in which surgery was combined with MSC therapy , proved good clinical outcome with no recurrence ***(Bey et al.,2007).***

There is a growing debate in the medical community over the efficacy and ethical implications of cell therapy. Much of the ethical debate revolves around the use of human fetal stem cells in treatment. While some cell therapy procedures have had proven success in clinical studies, others are still under continuous research to reach optimum benefits for all mankind***(Martin,2007).***

Aim of The Work